INVENTOR SEARCH

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=> file hcaplus
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FILE COVERS 1907 - 12 Sep 2007  VOL 147 ISS 12
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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos l27
L12             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  21339-55-9/RN
L13             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  26988-72-7/RN
L14             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  110117-83-4/RN
L15             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 OR L13 OR L14
L16             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  9014-51-1/RN
L17           637 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 OR METHYLTRYPTOPHAN/
                  OBI OR METHYL/OBI(W)TRYPTOPHAN/OBI
L18          8041 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR TDO/OBI(W)DIOXYGE
                  NASE/OBI OR TRYPTOPHAN/OBI(W)(PYRROLASE/OBI OR HYDROXYLAS
                  E/OBI OR DIOXYGENASE/OBI OR PEROXIDASE/OBI OR OXYGENASE/O
                  BI)OR INDOLEMINE/OBI(W)DIOXYGENASE/OBI OR TRYPTOPHAN/OBI(
                  W)2/OBI(W)3/OBI(W)DIOXYGENASE/OBI OR INDO/OBI
L23            98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24           290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L25            44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 AND L24
L26            32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L18
L27             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L17


=> file wpix
FILE 'WPIX' ENTERED AT 14:47:03 ON 12 SEP 2007
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FILE LAST UPDATED:                          11 SEP 2007   <20070911/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE:     200758      <200758/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> IPC Reform backfile reclassification has been loaded to 31 May
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    2007. No update date (UP) has been created for the reclassified
    documents, but they can be identified by 20060101/UPIC and
    20061231/UPIC and 20060601/UPIC. <<<

>>> Indian patent publication number format enhanced in DWPI - see NEWS <<
<

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http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
    PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

=> d que nos l34
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L33           14 SEA FILE=WPIX ABB=ON  PLU=ON  L23 AND L24
L34            6 SEA FILE=WPIX ABB=ON  PLU=ON  L33 AND L29


=> file japio
FILE 'JAPIO' ENTERED AT 14:47:14 ON 12 SEP 2007
COPYRIGHT (C) 2007 Japanese Patent Office (JPO)- JAPIO

FILE LAST UPDATED: 10 SEP 2007       <20070910/UP>
FILE COVERS APRIL 1973 TO MAY 31, 2007

>>> GRAPHIC IMAGES AVAILABLE <<<

=> d que nos l39
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L39            0 SEA FILE=JAPIO ABB=ON  PLU=ON  L23 AND L24


=> file medline
FILE 'MEDLINE' ENTERED AT 14:47:24 ON 12 SEP 2007

 FILE LAST UPDATED: 11 Sep 2007 (20070911/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> d que nos l46
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L45           37 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L24
L46            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L45 AND L29
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=> file biosis
FILE 'BIOSIS' ENTERED AT 14:47:44 ON 12 SEP 2007
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FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 5 September 2007 (20070905/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926
through 1968.  These records have been re-indexed to match current
BIOSIS indexing.

=> d que nos l54
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L53           46 SEA FILE=BIOSIS ABB=ON  PLU=ON  L23 AND L24
L54            3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L53 AND L29


=> file embase
FILE 'EMBASE' ENTERED AT 14:47:54 ON 12 SEP 2007
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 FILE COVERS 1974 TO 12 Sep 2007 (20070912/ED)

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos l62
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L61           37 SEA FILE=EMBASE ABB=ON  PLU=ON  L23 AND L24
L62            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L61 AND L29


=> file hcaplus medline biosis wpix embase
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=> dup rem l27 l46 l54 l34 l62
PROCESSING COMPLETED FOR L27
PROCESSING COMPLETED FOR L46
PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L62
L64           15 DUP REM L27 L46 L54 L34 L62 (9 DUPLICATES REMOVED)
                 ANSWERS '1-5' FROM FILE HCAPLUS
                 ANSWERS '6-10' FROM FILE MEDLINE
                 ANSWER '11' FROM FILE BIOSIS
                 ANSWERS '12-13' FROM FILE WPIX
                 ANSWERS '14-15' FROM FILE EMBASE

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L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  26988-72-7/RN
L14            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  110117-83-4/RN
L15            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 OR L13 OR L14
L16            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  9014-51-1/RN
L17          637 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 OR METHYLTRYPTOPHAN/
                 OBI OR METHYL/OBI(W)TRYPTOPHAN/OBI
L18         8041 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR TDO/OBI(W)DIOXYGE
                 NASE/OBI OR TRYPTOPHAN/OBI(W)(PYRROLASE/OBI OR HYDROXYLAS
                 E/OBI OR DIOXYGENASE/OBI OR PEROXIDASE/OBI OR OXYGENASE/O
                 BI)OR INDOLEMINE/OBI(W)DIOXYGENASE/OBI OR TRYPTOPHAN/OBI(
                 W)2/OBI(W)3/OBI(W)DIOXYGENASE/OBI OR INDO/OBI
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L25           44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 AND L24
L26           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L18
L27            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L17
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L33           14 SEA FILE=WPIX ABB=ON  PLU=ON  L23 AND L24
L34            6 SEA FILE=WPIX ABB=ON  PLU=ON  L33 AND L29
L45           37 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L24
L46            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L45 AND L29
L53           46 SEA FILE=BIOSIS ABB=ON  PLU=ON  L23 AND L24
L54            3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L53 AND L29
L61           37 SEA FILE=EMBASE ABB=ON  PLU=ON  L23 AND L24
L62            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L61 AND L29
L64           15 DUP REM L27 L46 L54 L34 L62 (9 DUPLICATES REMOVED)


=> d ibib abs l64 1-15

L64  ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2007:790312  HCAPLUS  Full-text
DOCUMENT NUMBER:          147:187318
TITLE:                    Indoleamine 2,3-dioxygenase inhibitor for
                          enhancing immune response against tumor or
                          infection and tryptophan metabolic product for
                          suppressing immune response against transplant
                          rejection and autoimmune disease
INVENTOR(S):              Chen, Wei; Blazar, Bruce R.; Munn, David
                          ; Mellor, Andrew
PATENT ASSIGNEE(S):       Medical College of Georgia Research Institute,
                          Inc., USA
SOURCE:                   PCT Int. Appl., 93pp.
```

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007081878	A2	20070719	WO 2007-US404	200701 05

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-756861P P 200601 07

AB The present invention provides methods for the control of the generation of regulatory T cells (Tregs) and uses thereof. Indoleamine 2,3-dioxygenase inhibitor e.g. 1-methyl-tryptophan is used to reduce immunosuppression mediated by regulatory T cells and to enhance immune response to vaccine, e.g. tumor or viral antigen. The invention also uses metabolic product of tryptophan for inducing regulatory T cells to increase immunosuppression and antigen tolerance to prevent and treat allograft or transplant rejection and autoimmune disease.

L64 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2007:483054 HCAPLUS Full-text
DOCUMENT NUMBER: 146:475678
TITLE: Indoleamine 2,3-dioxygenase modulation by TLR ligands and immunomodulatory uses thereof
INVENTOR(S): **Mellor, Andrew; Munn, David**
PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007050405	A2	20070503	WO 2006-US40796	200610 20

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-729041P P 200510 21

AB The induction of indoleamine 2,3-dioxygenase (IDO) in an IDO-competent subset of dendritic cells by TLR ligands, including TLR9 ligands, and various uses thereof, are presented. Also presented are e.g. a method for enhancing an immune response by administration of a TLR9 agonist and an IDO inhibitor.

L64 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:1019533 HCAPLUS Full-text
DOCUMENT NUMBER: 141:420433
TITLE: Use of inhibitors of indoleamine-2,3-dioxygenase in combination with other therapeutic modalities in the treatment of cancer and infection
INVENTOR(S): **Munn, David; Mellor, Andrew**
PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004234623	A1	20041125	US 2004-780797	200402 17
US 2005186289	A1	20050825	US 2004-780150	200402 17

PRIORITY APPLN. INFO.: US 2003-459489P P 200304 01
US 2004-538647P P 200401 22

AB The invention discloses a method for treating a subject with a cancer or an infection, the method including administering an inhibitor of indoleamine-2,3-dioxygenase (IDO) in an amount effective to reverse IDO-mediated immunosuppression, and administering at least one addnl. therapeutic agent,

wherein the administration of the inhibitor of IDO and the at least one addnl. therapeutic agent demonstrate therapeutic synergy.

L64 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1999:388082 HCAPLUS Full-text
DOCUMENT NUMBER: 131:35866
TITLE: Regulation of T cell-mediated immunity by tryptophan
INVENTOR(S): **Munn, David; Mellor, Andrew**
PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929310	A2	19990617	WO 1998-US25840	19981204
WO 9929310	A3	20000106		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9916285	A	19990628	AU 1999-16285	19981204
US 6395876	B1	20020528	US 1998-205939	19981204
US 6451840	B1	20020917	US 1998-206274	19981204
US 2001001040	A1	20010510	US 2000-727055	20001130
US 6482416	B2	20021119		
US 2002155104	A1	20021024	US 2002-112362	20020328
US 7160539	B2	20070109		
US 2007077224	A1	20070405	US 2006-602930	20061121
US 2007077234	A1	20070405	US 2006-603291	20061121
PRIORITY APPLN. INFO.:			US 1997-67610P P	19971205

US 1998-80380P	P	199804 01
US 1998-80384P	P	199804 01
US 1998-206274	A3	199812 04
WO 1998-US25840	W	199812 04
US 2002-112362	A3	200203 28

AB A mechanism of macrophage-induced T cell suppression is the selective elimination of tryptophan and/or increase in one or more tryptophan metabolites within the local macrophage microenvironment. Studies demonstrate that expression of IDO (indoleamine 2,3-dioxygenase) can serve as a marker of suppression of T cell activation, and may play a significant role in allogeneic pregnancy and therefore other types of transplantation, and that inhibitors of IDO can be used to activate T cells and therefore enhance T cell activation when the T cells are suppressed by pregnancy, malignancy or a virus such as HIV. Inhibiting tryptophan degradation (and thereby increasing tryptophan concentration while decreasing tryptophan metabolite concentration), or supplementing tryptophan concentration, can therefore be used in addition to, or in place of, inhibitors of IDO. Similarly, increasing tryptophan degradation (thereby, decreasing tryptophan concentration and increasing tryptophan metabolite concentration), for example, by increasing IDO concentration or IDO activity, can suppress T cells. Although described particularly with reference to IDO regulation, one can instead manipulate local tryptophan concns., and/or modulate the activity of the high affinity tryptophan transporter, and/or administer other tryptophan degrading enzymes. Regulation can be further manipulated using cytokines such as macrophage colony stimulating factor, interferon gamma, alone or in combination with antigen or other cytokines.

L64 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:818069 HCAPLUS Full-text
DOCUMENT NUMBER: 139:322295
TITLE: Antigen-presenting cell populations and their use as reagents for enhancing or reducing immune tolerance
INVENTOR(S): **Mellor, Andrew L.; Munn, David H.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003194803	A1	20031016	US 2002-121909	200204 12
CA 2483451	A1	20031023	CA 2002-2483451	200204 12
WO 2003087347	A1	20031023	WO 2002-US11319	200204 12
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002307243	A1	20031027	AU 2002-307243	200204 12
EP 1501918	A1	20050202	EP 2002-807233	200204 12
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2006292618	A1	20061228	US 2006-474162	200606 23
US 2007048769	A1	20070301	US 2006-474144	200606 23
PRIORITY APPLN. INFO.:			US 2002-121909 A	200204 12
			WO 2002-US11319 W	200204 12

AB The disclosed invention is based on the discovery that antigen-presenting cells (APCs) may be generated to have predetd. levels of expression of the intracellular enzyme, indoleamine 2,3-dioxygenase (IDO). Because expression of high levels of IDO is correlated with a reduced ability to stimulate T cell responses and an enhanced ability to induce immunol. tolerance, APCs having high levels of IDO may be used to increase tolerance in the immune system, as for example in transplant therapy or treatment of autoimmune disorders. For example, APCs having high levels of IDO, and expressing or loaded with at least one antigen from a donor tissue may be used to increase tolerance of the recipient to the donor's tissue. Alternatively, APCs having reduced levels of IDO expression and expressing or loaded with at least one antigen from a cancer or infectious pathogen may be used as vaccines to promote T cell responses and increase immunity.

L64 ANSWER 6 OF 15 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2007034353 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17234791
TITLE: Inhibition of indoleamine 2,3-dioxygenase in dendritic cells by stereoisomers of 1-methyl -tryptophan correlates with antitumor responses.
AUTHOR: Hou De-Yan; Muller Alexander J; Sharma Madhav D; DuHadaway James; Banerjee Tinku; Johnson Maribeth; **Mellor Andrew L**; Prendergast George C; **Munn David H**
CORPORATE SOURCE: Immunotherapy Center and Departments of Pediatrics, Medicine, and Biostatistics, Medical College of Georgia, Augusta, Georgia.
CONTRACT NUMBER: CA096651 (NCI)
CA103320 (NCI)
CA109542 (NCI)
CA112431 (NCI)
SOURCE: Cancer research, (2007 Jan 15) Vol. 67, No. 2, pp. 792-801.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 20 Jan 2007
Last Updated on STN: 21 Feb 2007
Entered Medline: 20 Feb 2007

AB Indoleamine 2,3-dioxygenase (IDO) is an immunosuppressive enzyme that contributes to tolerance in a number of biological settings. In cancer, IDO activity may help promote acquired tolerance to tumor antigens. The IDO inhibitor 1-methyl-tryptophan is being developed for clinical trials. However, 1-methyl -tryptophan exists in two stereoisomers with potentially different biological properties, and it has been unclear which isomer might be preferable for initial development. In this study, we provide evidence that the D and L stereoisomers exhibit important cell type-specific variations in activity. The L isomer was the more potent inhibitor of IDO activity using the purified enzyme and in HeLa cell-based assays. However, the D isomer was significantly more effective in reversing the suppression of T cells created by IDO-expressing dendritic cells, using both human monocyte-derived dendritic cells and murine dendritic cells isolated directly from tumor-draining lymph nodes. In vivo, the d isomer was more efficacious as an anticancer agent in chemo-immunotherapy regimens using cyclophosphamide, paclitaxel, or gemcitabine, when tested in mouse models of transplantable melanoma and transplantable and autochthonous breast cancer. The D isomer of 1-methyl-tryptophan specifically targeted the IDO gene because the antitumor effect of D-1-methyl-tryptophan was completely lost in mice with a disruption of the IDO gene (IDO-knockout mice). Taken together, our findings support the suitability of D-1-methyl-tryptophan for human trials aiming to assess the utility of IDO inhibition to block host-mediated immunosuppression and enhance antitumor immunity in the setting of combined chemo-immunotherapy regimens.

L64 ANSWER 7 OF 15 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002453562 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12209992
TITLE: Indoleamine 2,3-dioxygenase contributes to tumor cell

evasion of T cell-mediated rejection.
AUTHOR: Friberg Maria; Jennings Ronald; Alsarraj Marwan; Dessureault Sophie; Cantor Alan; Extermann Martine; **Mellor Andrew L**; **Munn David H**; Antonia Scott J
CORPORATE SOURCE: Department of Interdisciplinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL 33612, USA.
SOURCE: International journal of cancer. Journal international du cancer, (2002 Sep 10) Vol. 101, No. 2, pp. 151-5.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 6 Sep 2002
Last Updated on STN: 2 Oct 2002
Entered Medline: 1 Oct 2002

AB The priming of an appropriate anti-tumor T cell response rarely results in the rejection of established tumors. The characteristics of tumors that allow them to evade a T cell-mediated rejection are unknown for many tumors. We report on evidence that the expression of the immunosuppressive enzyme, indoleamine 2,3-dioxygenase (IDO) by mononuclear cells that invade tumors and tumor-draining lymph nodes, is 1 mechanism that may account for this observation. Lewis lung carcinoma (LLC) cells stimulated a more robust allogeneic T cell response in vitro in the presence of a competitive inhibitor of IDO, 1-**methyl tryptophan**. When administered in vivo this inhibitor also resulted in delayed LLC tumor growth in syngeneic mice. Our study provides evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggests the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy. Copyright 2002 Wiley-Liss, Inc.

L64 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1998378582 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9712583
TITLE: Prevention of allogeneic fetal rejection by tryptophan catabolism.
AUTHOR: **Munn D H**; Zhou M; Attwood J T; Bondarev I; Conway S J; Marshall B; Brown C; **Mellor A L**
CORPORATE SOURCE: Program in Molecular Immunology, Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, GA 30912, USA.
SOURCE: Science (New York, N.Y.), (1998 Aug 21) Vol. 281, No. 5380, pp. 1191-3.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 17 Sep 1998
Last Updated on STN: 17 Sep 1998
Entered Medline: 8 Sep 1998

AB In 1953 Medawar pointed out that survival of the genetically disparate (allogeneic) mammalian conceptus contradicts the laws of tissue transplantation. Rapid T cell-induced rejection of all allogeneic concepti

occurred when pregnant mice were treated with a pharmacologic inhibitor of indoleamine 2,3-dioxygenase (IDO), a tryptophan-catabolizing enzyme expressed by trophoblasts and macrophages. Thus, by catabolizing tryptophan, the mammalian conceptus suppresses T cell activity and defends itself against rejection.

L64 ANSWER 9 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2002470245 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12228717
TITLE: Potential regulatory function of human dendritic cells expressing indoleamine 2,3-dioxygenase.
AUTHOR: **Munn David H**; Sharma Madhav D; Lee Jeffrey R; Jhaver Kanchan G; Johnson Theodore S; Keskin Derin B; Marshall Brendan; Chandler Phillip; Antonia Scott J; Burgess Russell; Slingluff Craig L Jr; **Mellor Andrew L**
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, GA 30912, USA.. dmunn@mail.mcg.edu
CONTRACT NUMBER: AI44219 (NIAID)
AI44759 (NIAID)
HL60137 (NHLBI)
SOURCE: Science (New York, N.Y.), (2002 Sep 13) Vol. 297, No. 5588, pp. 1867-70.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 17 Sep 2002
Last Updated on STN: 8 Oct 2002
Entered Medline: 4 Oct 2002

AB Antigen-presenting cells (APCs) can induce tolerance or immunity. We describe a subset of human APCs that express indoleamine 2,3-dioxygenase (IDO) and inhibit T cell proliferation in vitro. IDO-positive APCs constituted a discrete subset identified by coexpression of the cell-surface markers CD123 and CCR6. In the dendritic cell (DC) lineage, IDO-mediated suppressor activity was present in fully mature as well as immature CD123+ DCs. IDO+ DCs could also be readily detected in vivo, which suggests that these cells may represent a regulatory subset of APCs in humans.

L64 ANSWER 10 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999242635 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10224276
TITLE: Inhibition of T cell proliferation by macrophage tryptophan catabolism.
AUTHOR: **Munn D H**; Shafizadeh E; Attwood J T; Bondarev I; Pashine A; **Mellor A L**
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, Georgia 30912, USA.. dmunn@mail.mcg.edu
CONTRACT NUMBER: K08 HL03395 (NHLBI)
R01 HL60137 (NHLBI)
R21 AI44759 (NIAID)
SOURCE: The Journal of experimental medicine, (1999 May 3)

Vol. 189, No. 9, pp. 1363-72.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 28 Jun 1999
Last Updated on STN: 28 Jun 1999
Entered Medline: 15 Jun 1999

AB We have recently shown that expression of the enzyme indoleamine 2, 3-dioxygenase (IDO) during murine pregnancy is required to prevent rejection of the allogeneic fetus by maternal T cells. In addition to their role in pregnancy, IDO-expressing cells are widely distributed in primary and secondary lymphoid organs. Here we show that monocytes that have differentiated under the influence of macrophage colony-stimulating factor acquire the ability to suppress T cell proliferation in vitro via rapid and selective degradation of tryptophan by IDO. IDO was induced in macrophages by a synergistic combination of the T cell-derived signals IFN-gamma and CD40-ligand. Inhibition of IDO with the 1-methyl analogue of tryptophan prevented macrophage-mediated suppression. Purified T cells activated under tryptophan-deficient conditions were able to synthesize protein, enter the cell cycle, and progress normally through the initial stages of G1, including upregulation of IL-2 receptor and synthesis of IL-2. However, in the absence of tryptophan, cell cycle progression halted at a mid-G1 arrest point. Restoration of tryptophan to arrested cells was not sufficient to allow further cell cycle progression nor was costimulation via CD28. T cells could exit the arrested state only if a second round of T cell receptor signaling was provided in the presence of tryptophan. These data reveal a novel mechanism by which antigen-presenting cells can regulate T cell activation via tryptophan catabolism. We speculate that expression of IDO by certain antigen presenting cells in vivo allows them to suppress unwanted T cell responses.

L64 ANSWER 11 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:278681 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100278681
TITLE: Cells expressing indoleamine 2,3-dioxygenase induce accelerated activation-induced T cell death (AICD).
AUTHOR(S): Keskin, D. B.; **Munn**, D.; **Mellor, A.** L.
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A349. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Jun 2001
Last Updated on STN: 19 Feb 2002

AB Cells expressing indoleamine 2,3-dioxygenase (IDO), which catabolizes tryptophan, suppress maternal T cell immunity directed against fetal alloantigens. To evaluate the mechanism by which IDO expression moderates T cell responses we generated IDO-expressing cell lines by transfecting murine

MB49 urinary bladder carcinoma and MC57C fibrosarcoma cell lines with DNA constructs containing murine IDO cDNA sequences. IDO expression in transfected cells was assessed by immunostaining and tryptophan depletion from culture medium. The ability of IDO-transfected cells to induce T cell proliferation was evaluated in co-cultures with H-2K b-specific T cells by staining splenocytes from T cell receptor transgenic mice with the dye CSFE. Measurements of the numbers of dividing T cells in co-cultures by flow cytometric methods showed that antigen presenting and T cell activation functions of IDO-transfected and vector-transfected cell lines were comparable. However, the majority of T cells that had undergone cell division in co-cultures containing IDO-expressing cells were not viable as assessed by Annexin V staining and other markers of apoptosis. Addition of excess tryptophan or 1-**methyl-tryptophan**, which inhibits IDO activity, to culture medium reversed the substantial decreases in T cell viability following activation by IDO-transfectants. We conclude that T cells activated in the presence of cells expressing IDO die following activation and proliferation due to reduced access to tryptophan. These findings suggest that IDO expression by antigen presenting cells in local tissue microenvironments may accelerate T cell death leading to induction of local tolerance. This hypothesis will be discussed in the context of tolerance induction allowing acceptance of foreign cells and tissues by immunocompetent hosts.

L64 ANSWER 12 OF 15 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-628259 [64] WPIX
CROSS REFERENCE: 2004-832914
DOC. NO. CPI: C2005-188484 [64]
TITLE: Augmenting rejection of cells by a patient and treating patient with infection involves the use of D isomer of inhibitor of indoleamine-2,3-dioxygenase
DERWENT CLASS: B05; C03
INVENTOR: **MELLOR A**; **MUNN D**
PATENT ASSIGNEE: (MEDI-N) MEDICAL COLLEGE GEORGIA RES INST
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20050186289	A1	20050825	(200564)*	EN	44	[11]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20050186289	A1 Provisional	US 2003-459489P	20030401
US 20050186289	A1 Provisional	US 2004-538647P	20040122
US 20050186289	A1	US 2004-780150	20040217

PRIORITY APPLN. INFO: US 2004-780150 20040217
US 2003-459489P 20030401
US 2004-538647P 20040122
AN 2005-628259 [64] WPIX
CR 2004-832914
AB US 20050186289 A1 UPAB: 20051223
NOVELTY - A method (M1) of augmenting rejection of cells by a patient involves administering a pharmaceutical composition (A) comprising a D isomer of an inhibitor of indoleamine-2,3-dioxygenase (IDO).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a method (M2) of treating a patient with an infection involving administering (A) optionally in combination with a vaccine; and
(2) a pharmaceutical composition (A1) comprising a D isomer of an inhibitor of indoleamine-2,3-dioxygenase and at least one additional therapeutic agent (C2).
ACTIVITY - Cytostatic; Virucide; Anti-HIV; Antiparasitic; Antibacterial; Antimalarial; Tuberculostatic; Antitubercular. B16F10 melanomas were implanted in C57BL/6 mice, then 7 days later mice were treated with 1-methyl-tryptophan (1-MT) or vehicle control (administered by subcutaneous (SQ) continuous infusion using implantable co-polymer pellets as given in Munn et al., Science 1998;281:1191-1193). The initial studies used the DL racemic form of 1 MT, at a total dose of 20 mg per mouse per day. In this established-tumor model, 1MT alone had no effect. When the established host/tumor milieu was transiently perturbed by a single dose of total-body radiation (500 cGy) or cyclophosphamide (150 mg/kgx1 dose), 1MT acted synergistically with both interventions, to significantly reduce tumor growth. Although the combination was not curative, this degree of growth delay was comparable to that seen with other immunologic interventions in this aggressive tumor model. Identical experiments performed in immunodeficient hosts showed no enhancing effect of 1MT over cyclophosphamide alone, indicating that the effect of 1MT was entirely immunologically mediated. Finally, the (D)-isomer of 1MT was found to be effective at one quarter the dose used for the racemic preparation. The radiation studies were replicated using a similar experimental design. The 1MT alone had no effect, but with the combination of the (D)-isomer of 1MT and radiation showed enhanced effect over radiation alone.
MECHANISM OF ACTION - Inhibitor of indoleamine-2,3- dioxygenase (IDO); Immune response stimulator. Cultured human dendritic cells (DCs) enriched for IDO expression were prepared as described by Munn et al., Science 1998;281:1191-1193 and DCs were used as stimulators in allogeneic mixed-leukocyte reactions (MLRs), with allogeneic lymphocytes as responder cells. The ability of 1-methyl- tryptophan (1-MT) to inhibit IDO-mediated suppression was measured as the amount of T cell proliferation. It was found that 1-methyl-D-tryptophan was significantly more effective than 1-methyl-L-tryptophan at reversing IDO-mediated suppression.
USE - For augmenting rejection of cells e.g. tumor cells e.g. a cancer such as melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer and Kaposi's sarcoma and cells infected by a virus (e.g. human immunodeficiency virus (HIV) or cytomegalovirus (HCMV)), an intracellular parasite (e.g. Leishmania donovani, Leishmania tropica, Leishmania major, Leishmania aethiopica, Leishmania mexicana, Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, and Plasmodium malariae), or an intracellular bacteria (e.g. Mycobacterium leprae, Mycobacterium tuberculosis, Listeria monocytogenes, and Toxplasma gondii) and for stimulating an immune response; enhancing the signal in a mixed leukocyte response (MLR); increasing T cell activation by an antigen-presenting cell; reversing the immunosuppressed state in a subject with HIV; and treating a patient with an infection e.g. an infection with the HIV virus, infection with a CMV virus, infection with an intracellular parasite, and infection with a bacteria; reducing immunosuppression mediated by an antigen presenting cell that expresses indoleamine-2,3-dioxygenase (IDO); preventing the development of immunosuppression mediated by the antigen presenting cell in a patient that has undergone a bone marrow transplant; delaying the relapse or progression of a tumor in a patient; treating a patient suffering from a neoplastic condition (claimed).
ADVANTAGE - The non-physiologic D-isomer of the inhibitor is much more effective in reversing IDO-mediated immune suppression than either the physiologic L-isomer or a racemic mixture. The reversal of IDO-mediated immune suppression observed with a D-isomer of an IDO inhibitor is greater than that observed with an equimolar mixture of the D-isomer and the L-isomer.

L64 ANSWER 13 OF 15 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-119014 [11] WPIX
CROSS REFERENCE: 1999-394927; 1999-394973; 2002-546166; 2002-546465; 2003-227919; 2003-228111
DOC. NO. CPI: C2003-030680 [11]
TITLE: Increasing T cell activation by an antigen-bearing cell for altering maternal tolerance of pregnancy, by administering to a subject a pharmaceutical composition comprising indoleamine-2,3-dioxygenase inhibitor
DERWENT CLASS: B02
INVENTOR: **MELLOR A; MUNN D**
PATENT ASSIGNEE: (MEDI-N) MEDICAL COLLEGE GEORGIA RES INST
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 6451840	B1	20020917	(200311)*	EN	27	[11]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6451840	B1 Provisional	US 1997-67610P	19971205
US 6451840	B1 Provisional	US 1998-80380P	19980401
US 6451840	B1 Provisional	US 1998-80384P	19980401
US 6451840	B1	US 1998-206274	19981204

PRIORITY APPLN. INFO: US 1998-206274 19981204
US 1997-67610P 19971205
US 1998-80380P 19980401
US 1998-80384P 19980401

AN 2003-119014 [11] WPIX
CR 1999-394927; 1999-394973; 2002-546166; 2002-546465; 2003-227919; 2003-228111
AB US 6451840 B1 UPAB: 20050528
NOVELTY - Increasing (M) T cell activation by an antigen-bearing cell, involves administering an amount of a pharmaceutical composition (I) comprising an inhibitor of indoleamine-2,3- dioxygenase.
ACTIVITY - Anti-HIV; Antiinflammatory; Cytostatic. Inhibition of tumor growth by administration of indoleamine-2,3-dioxygenase (IDO) inhibitor was as follows. Tumor-bearing hosts were treated with the IDO inhibitor 1- **methyl-tryptophan**. MB49 tumor cells (1x106) were injected subcutaneously into syngeneic C57/B16 host. Pellets containing 1-**methyl-tryptophan** (0.9 mg/hour, 7-day release) were implanted at the time of tumor cell inoculation. By day 10, all animals had evidence of initial tumor formation (palpable mass). By day 15, control animals were visibly ill and the experiment was terminated. Animals were sacrificed on day 11-15 for histologic examination. The results showed that, administration of 1-**methyl-tryptophan** significantly reduced tumor growth in immunocompetent, syngeneic hosts, compared to vehicle control.
MECHANISM OF ACTION - Inhibitor of indoleamine-2,3- dioxygenase (claimed); Enhancer of T cell activation; Inducer of rejection of a fetus; Inhibitor of tumor growth.
USE - (M) is useful for increasing T cell activation by an antigen-bearing cell in a subject, preferably human (claimed). (M) is useful to enhance T cell activation when the T cells are suppressed by pregnancy, malignancy or a virus such as human immunodeficiency virus (HIV). (M) is useful for altering

maternal tolerance of pregnancy, to affect infection by certain viruses such as HIV and inflammation, to induce rejection of a fetus, to terminate or prevent pregnancy, or to inhibit tumor growth.

L64 ANSWER 14 OF 15 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007229728 EMBASE Full-text
TITLE: Indoleamine 2,3-dioxygenase and tumor-induced tolerance.
AUTHOR: **Munn D.H.; Mellor A.L.**
CORPORATE SOURCE: D.H. Munn, Immunotherapy Program, MCG Cancer Center, Augusta, GA 30912, United States. dmunn@mail.mcg.edu
SOURCE: Journal of Clinical Investigation, (1 May 2007) Vol. 117, No. 5, pp. 1147-1154. .
Refs: 125
ISSN: 0021-9738 E-ISSN: 1558-8238 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jun 2007
Last Updated on STN: 29 Jun 2007

AB Tumors arise from normal cells of the body through genetic mutation. Although such genetic mutation often leads to the expression of abnormal antigens, the immune system fails to respond effectively to these antigens; that is, it is tolerant of these antigens. This acquired state of tolerance must be overcome for cancer immunotherapy to succeed. Indoleamine 2,3-dioxygenase (IDO) is one molecular mechanism that contributes to tumor-induced tolerance. IDO helps create a tolerogenic milieu in the tumor and the tumor-draining lymph nodes, both by direct suppression of T cells and enhancement of local Treg-mediated immunosuppression. It can also function as an antagonist to other activators of antitumor immunity. Therefore, strategies to block IDO might enhance the effectiveness of tumor immunotherapy.

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ACCESSION NUMBER: 1999353415 EMBASE Full-text
TITLE: Tryptophan catabolism and T-cell tolerance: Immunosuppression by starvation?.
AUTHOR: **Mellor A.L.; Munn D.H.**
CORPORATE SOURCE: A.L. Mellor, Molecular Immunology Program, Inst. of Molecular Med. and Genet., Medical College of Georgia, Augusta, GA 30912, United States. mellor@immag.mcg.edu
SOURCE: Immunology Today, (1999) Vol. 20, No. 10, pp. 469-473. .
Refs: 42
ISSN: 0167-5699 CODEN: IMTOD8
PUBLISHER IDENT.: S 0167-5699(99)01520-0
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
ENTRY DATE: Entered STN: 29 Oct 1999
Last Updated on STN: 29 Oct 1999

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FILE 'MEDLINE' ENTERED AT 14:51:35 ON 12 SEP 2007

 FILE LAST UPDATED: 11 Sep 2007 (20070911/UP).  FILE COVERS 1950 TO DATE.
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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> d que nos l47
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L40          461 SEA FILE=MEDLINE ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L41         6818 SEA FILE=MEDLINE ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR
                 TRYPTOPHAN(W)(PYRROLASE OR HYDROXYLASE OR DIOXYGENASE OR
                 PEROXIDASE OR OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR
                 TRYPTOPHAN(W)2(W)3(W)DIOXYGENASE OR INDO
L42           51 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND L41
L43      1982664 SEA FILE=MEDLINE ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR
                 SARCOMA? OR NEOPLASM? OR LYMPHOMA? OR TUMOR?
L44            8 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND L43
L45           37 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L24
L46            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L45 AND L29
L47            7 SEA FILE=MEDLINE ABB=ON  PLU=ON  L44 NOT L46


=> file biosis
FILE 'BIOSIS' ENTERED AT 14:51:45 ON 12 SEP 2007
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FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 5 September 2007 (20070905/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926
through 1968.  These records have been re-indexed to match current
BIOSIS indexing.

=> d que nos l55
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L48          616 SEA FILE=BIOSIS ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L49        13004 SEA FILE=BIOSIS ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR
                 TRYPTOPHAN(W)(PYRROLASE OR HYDROXYLASE OR DIOXYGENASE OR
                 PEROXIDASE OR OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR
                 TRYPTOPHAN(W)2(W)3(W)DIOXYGENASE OR INDO
L50           17 SEA FILE=BIOSIS ABB=ON  PLU=ON  L48 AND L49
L51      1583882 SEA FILE=BIOSIS ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR
                 SARCOMA? OR NEOPLASM? OR LYMPHOMA? OR TUMOR?
L52            2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L50 AND L51
L53           46 SEA FILE=BIOSIS ABB=ON  PLU=ON  L23 AND L24
L54            3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L53 AND L29
L55            1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L52 NOT L54


=> file embase
FILE 'EMBASE' ENTERED AT 14:51:57 ON 12 SEP 2007
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FILE COVERS 1974 TO 12 Sep 2007 (20070912/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d que nos l63
L23           98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24          290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L29           85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L56          547 SEA FILE=EMBASE ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                 METHYL(W)TRYPTOPHAN
L57         5445 SEA FILE=EMBASE ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR
                 TRYPTOPHAN(W)(PYRROLASE OR HYDROXYLASE OR DIOXYGENASE OR
                 PEROXIDASE OR OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR
                 TRYPTOPHAN(W)2(W)3(W)DIOXYGENASE OR INDO
L58           24 SEA FILE=EMBASE ABB=ON  PLU=ON  L56 AND L57
L59      1446540 SEA FILE=EMBASE ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR
                 SARCOMA? OR NEOPLASM? OR LYMPHOMA? OR TUMOR?
L60            2 SEA FILE=EMBASE ABB=ON  PLU=ON  L58 AND L59
L61           37 SEA FILE=EMBASE ABB=ON  PLU=ON  L23 AND L24
L62            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L61 AND L29
L63            1 SEA FILE=EMBASE ABB=ON  PLU=ON  L60 NOT L62


=> file hcaplus medline biosis embase
FILE 'HCAPLUS' ENTERED AT 14:52:32 ON 12 SEP 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 14:52:32 ON 12 SEP 2007

FILE 'BIOSIS' ENTERED AT 14:52:32 ON 12 SEP 2007
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FILE 'EMBASE' ENTERED AT 14:52:32 ON 12 SEP 2007
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=> dup rem l28 l47 l55 l63
PROCESSING COMPLETED FOR L28
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L55
PROCESSING COMPLETED FOR L63
L65           13 DUP REM L28 L47 L55 L63 (0 DUPLICATES REMOVED)
                 ANSWERS '1-4' FROM FILE HCAPLUS
                 ANSWERS '5-11' FROM FILE MEDLINE
                 ANSWER '12' FROM FILE BIOSIS
                 ANSWER '13' FROM FILE EMBASE

=> d que nos l65
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  21339-55-9/RN
L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  26988-72-7/RN
L14            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  110117-83-4/RN
L15            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 OR L13 OR L14
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L17         637 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 OR METHYLTRYPTOPHAN/
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L18        8041 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR TDO/OBI(W)DIOXYGE
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                BI)OR INDOLEMINE/OBI(W)DIOXYGENASE/OBI OR TRYPTOPHAN/OBI(
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                OR TUMOR?/OBI
L20          39 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L18
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L22           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND (1840-2003)/PRY,
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L23          98 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MUNN D?/AU
L24         290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MELLOR A?/AU
L25          44 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 AND L24
L26          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L18
L27           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L17
L28           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 NOT L27
L29          85 SEA FILE=WPIX ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                METHYL(W)TRYPTOPHAN
L40         461 SEA FILE=MEDLINE ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                METHYL(W)TRYPTOPHAN
L41        6818 SEA FILE=MEDLINE ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR
                TRYPTOPHAN(W)(PYRROLASE OR HYDROXYLASE OR DIOXYGENASE OR
                PEROXIDASE OR OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR
                TRYPTOPHAN(W)2(W)3(W)DIOXYGENASE OR INDO
L42          51 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND L41
L43     1982664 SEA FILE=MEDLINE ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR
                SARCOMA? OR NEOPLASM? OR LYMPHOMA? OR TUMOR?
L44           8 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND L43
L45          37 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L24
L46           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L45 AND L29
L47           7 SEA FILE=MEDLINE ABB=ON  PLU=ON  L44 NOT L46
L48         616 SEA FILE=BIOSIS ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                METHYL(W)TRYPTOPHAN
L49       13004 SEA FILE=BIOSIS ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR
                TRYPTOPHAN(W)(PYRROLASE OR HYDROXYLASE OR DIOXYGENASE OR
                PEROXIDASE OR OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR
                TRYPTOPHAN(W)2(W)3(W)DIOXYGENASE OR INDO
L50          17 SEA FILE=BIOSIS ABB=ON  PLU=ON  L48 AND L49
L51     1583882 SEA FILE=BIOSIS ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR
                SARCOMA? OR NEOPLASM? OR LYMPHOMA? OR TUMOR?
L52           2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L50 AND L51
L53          46 SEA FILE=BIOSIS ABB=ON  PLU=ON  L23 AND L24
L54           3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L53 AND L29
L55           1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L52 NOT L54
L56         547 SEA FILE=EMBASE ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR
                METHYL(W)TRYPTOPHAN
L57        5445 SEA FILE=EMBASE ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR
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L58          24 SEA FILE=EMBASE ABB=ON  PLU=ON  L56 AND L57
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                SARCOMA? OR NEOPLASM? OR LYMPHOMA? OR TUMOR?
L60           2 SEA FILE=EMBASE ABB=ON  PLU=ON  L58 AND L59
L61          37 SEA FILE=EMBASE ABB=ON  PLU=ON  L23 AND L24
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L62             5 SEA FILE=EMBASE ABB=ON  PLU=ON  L61 AND L29
L63             1 SEA FILE=EMBASE ABB=ON  PLU=ON  L60 NOT L62
L65            13 DUP REM L28 L47 L55 L63 (0 DUPLICATES REMOVED)


=> d l65 ibib abs hitrn 1-4;d l65 5-13 iall

L65  ANSWER 1 OF 13  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:927197  HCAPLUS  Full-text
DOCUMENT NUMBER:          141:388648
TITLE:                    Novel ido (indoleamine 2,3-dioxygenase)
                          inhibitors and methods of use
INVENTOR(S):              Prendergast, George C.; Muller, Alexander J.;
                          Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S):       Lankenau Institute for Medical Research, USA
SOURCE:                   PCT Int. Appl., 115 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE       APPLICATION NO.          DATE
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     WO 2004094409         A1    20041104   WO 2004-US5154
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         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
             SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
             VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
             DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
             SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
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     CA 2520586            A1    20041104   CA 2004-2520586
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     EP 1606285            A1    20051221   EP 2004-713430
                                                                    200402
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         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
             PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,
             SK
     CN 1795187            A     20060628   CN 2004-80008331
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     CN 1794986            A     20060628   CN 2004-80014321
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JP 2006521377	T	20060921	JP 2006-508788 <--	20040220
US 2007173524	A1	20070726	US 2006-550444 <--	20060601
PRIORITY APPLN. INFO.:			US 2003-458162P <--	P 20030327
			US 2003-527449P <--	P 20031205
			WO 2004-US5154	W 20040220

OTHER SOURCE(S): MARPAT 141:388648

AB Novel inhibitors of indoleamine 2,3-dioxygenase (IDO) activity are provided. In yet another embodiment of the present invention, a combination treatment protocol comprising administration of an IDO inhibitor with a signal transduction inhibitor (STI) or chemotherapeutic agent is provided, which is effective for suppressing tumor growth. In still another embodiment of the present invention, a combination treatment protocol is provided for the treatment of a chronic viral infection, comprising the administration of an IDO inhibitor and a chemotherapeutic agent.

IT 9014-51-1, Indoleamine 2,3-dioxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel indoleamine dioxygenase inhibitors for treatment of tumors and viral infections and combination with chemotherapeutic agents and signal transduction inhibitors)

IT 21339-55-9, 1-Methyltryptophan 26988-72-7
, 1-DL-Methyltryptophan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel indoleamine dioxygenase inhibitors for treatment of tumors and viral infections and combination with chemotherapeutic agents and signal transduction inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2004:927043 HCAPLUS Full-text
DOCUMENT NUMBER:	141:388646
TITLE:	Novel methods for the treatment of cancer and viral infections
INVENTOR(S):	Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S):	Lankenau Institute for Medical Research, USA
SOURCE:	PCT Int. Appl., 65 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093871	A1	20041104	WO 2004-US5155	200402 20
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2520172	A1	20041104	CA 2004-2520172	200402 20
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EP 1613308	A1	20060111	EP 2004-713378	200402 20
			<--	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1795187	A	20060628	CN 2004-80008331	200402 20
			<--	
CN 1794986	A	20060628	CN 2004-80014321	200402 20
			<--	
JP 2006521378	T	20060921	JP 2006-508789	200402 20
			<--	
US 2007099844	A1	20070503	US 2006-551151	200605 18
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PRIORITY APPLN. INFO.:			US 2003-458162P P	200303 27
			<--	
			US 2003-527449P P	200312 05
			<--	
			WO 2004-US5155 W	200402 20

AB Compns. and methods for the treatment of malignancy and chronic viral infection are disclosed. A method is claimed for treating a cancer comprising

administering at least one indoleamine 2,3-dioxygenase (IDO) inhibitor and at least one signal transduction inhibitor (STI). A method is claimed for treating a cancer comprising administering at least one immunomodulator, other than IDO inhibitor, and at least one cytotoxic chemotherapeutic agent or at least one STI. A method for treating a chronic viral infection in a patient is claimed comprising administering at least one IDO inhibitor and at least one chemotherapeutic agent. Pharmaceutical compns. containing compds. of the invention for treating cancer and viral infections are also claimed.

IT 9014-51-1, Indoleamine 2,3-dioxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treatment of cancer and viral infections using indoleamine 2,3-dioxygenase inhibitors, signal transduction inhibitors, chemotherapeutic agents, and immunomodulators)

IT 21339-55-9, 1-Methyltryptophan 26988-72-7
, 1-Methyl-DL-tryptophan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer and viral infections using indoleamine 2,3-dioxygenase inhibitors, signal transduction inhibitors, chemotherapeutic agents, and immunomodulators)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:790660 HCAPLUS Full-text
DOCUMENT NUMBER: 133:349121
TITLE: Methods for increasing T cell proliferation
INVENTOR(S): Van, Den Eynde Benoit; Bilsborough, Janine; Boon-Falleur, Thierry
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066764	A1	20001109	WO 2000-US12118	200005 03
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W: AU, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1185687	A1	20020313	EP 2000-928796	200005 03
			<--	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1999-132219P	P 199905 03
			<--	
			WO 2000-US12118	W 200005

03

<--

AB The invention provides methods and compns. for increasing T cell proliferation using tryptophan enhancing agents. T cell proliferation can be increased in vitro by addition of tryptophan enhancing agents to T cell culture, or in vivo by administration of tryptophan enhancing agents. Also provided are methods for diagnosing and treating disorders characterized by constitutive expression of indoleamine-2,3-dioxygenase. Compns. and apparatus relating to the methods also are provided.

IT 9014-51-1, Indoleamine 2,3-dioxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; methods for increasing T cell proliferation)

IT 26988-72-7, 1-Methyl-DL-tryptophan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for increasing T cell proliferation)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:457008 HCAPLUS Full-text
DOCUMENT NUMBER: 63:57008
ORIGINAL REFERENCE NO.: 63:10439g-h,10440a
TITLE: A **tryptophan hydroxylase** in cell-free extracts of malignant mouse mast cells
AUTHOR(S): Lovenberg, Walter; Levine, Robert J.; Sjoerdsma, Albert
CORPORATE SOURCE: Natl. Heart Inst., Bethesda, MD
SOURCE: Biochemical Pharmacology (1965), 14(5), 887-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hydroxylation of tryptophan (I) and phenylalanine (II) at physiol. levels was observed in a cell-free system of the mouse mast cells supplemented with Fe2+ and 6,7-dimethyl-2-amino-4- hydroxytetrahydropteridine (III) or tetrahydrofolic acid (IV). For these expts., mice (Balb/c + DBA/2; F1 hybrids) bearing the transplantable tumor P815 in the ascitic form during generations 415-45 were used. The broken cell extract of the mast cells was centrifuged at 100,000 g for 60 min. and the protein was precipitated from the supernatant fraction with (NH4)2SO4 (20-40% saturation). With a cofactor concentration of 10-4M, enzyme activity of hydroxylating I after dialysis of the protein was 2-3-fold greater with III than with IV. Optimum pH of 6.5-7.5 and formation of 5-hydroxytryptophan at a constant rate for up to 90 min. were observed. II was hydroxylated at a rate similar to that of I and its enzyme had a similar cofactor requirement. With the addition of cofactors, II was hydroxylated rapidly in a rat liver supernatant fraction, but hydroxylation of I was not detected. The 2 enzymes could be distinguished since Km values for L-tryptophan were 6.8 + 10-3 M for the rat liver enzyme (Renson, et al., CA 57, 7617c) and about 10-5M for the mast cell enzyme. 2-Propyl-3,4-dihydroxyphenylacetamide and -methyl-3,4-dihydroxyphenylalanine inhibited the hydroxylation reaction of the mast cell enzyme by 90% and 50%, resp., at 5 + 10-4M. Since intact cells hydroxylated I without the addition of cofactors, it appeared that either cofactors were localized at a specific site within the intact cell or some stabilizing factor was destroyed.

L65 ANSWER 5 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2004490921 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15448685
TITLE: 4-1BB-mediated immunotherapy of rheumatoid arthritis.
AUTHOR: Seo Su K; Choi Jae H; Kim Young H; Kang Woo J; Park Hye Y; Suh Jae H; Choi Beom K; Vinay Dass S; Kwon Byoung S
CORPORATE SOURCE: The Immunomodulation Research Center, University of Ulsan, 29 Mukeo-Dong, Nam-ku, Ulsan 680-749, Korea.
CONTRACT NUMBER: P30EY002377 (NEI)
R01EY013325 (NEI)
SOURCE: Nature medicine, (2004 Oct) Vol. 10, No. 10, pp. 1088-94. Electronic Publication: 2004-09-26.
Journal code: 9502015. ISSN: 1078-8956.
COMMENT: Comment in: Nat Med. 2004 Oct;10(10):1047-9. PubMed ID: 15459704
Erratum in: Nat Med. 2004 Nov;10(11):1261
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 2 Oct 2004
Last Updated on STN: 19 Jan 2005
Entered Medline: 18 Jan 2005

ABSTRACT:
Collagen type II-induced arthritis is a CD4(+) T-cell-dependent chronic inflammation in susceptible DBA/1 mice and represents an animal model of human rheumatoid arthritis. We found that development of this condition, and even established disease, are inhibited by an agonistic anti-4-1BB monoclonal antibody. Anti-4-1BB suppressed serum antibodies to collagen type II and CD4(+) T-cell recall responses to collagen type II. Crosslinking of 4-1BB evoked an antigen-specific, active suppression mechanism that differed from the results of blocking the interaction between 4-1BB and its ligand, 4-1BBL. Anti-4-1BB monoclonal antibodies induced massive, antigen-dependent clonal expansion of CD11c(+)CD8(+) T cells and accumulation of indoleamine 2,3-dioxygenase in CD11b(+) monocytes and CD11c(+) dendritic cells. Both anti-interferon-gamma and 1-**methyltryptophan**, a pharmacological inhibitor of indoleamine 2,3-dioxygenase, reversed the anti-4-1BB effect. We conclude that the suppression of collagen-induced arthritis was caused by an expansion of new CD11c(+)CD8(+) T cells, and that interferon-gamma produced by these cells suppresses antigen-specific CD4(+) T cells through an indoleamine 2,3-dioxygenase-dependent mechanism.

CONTROLLED TERM: Animals
Antibodies, Monoclonal: IM, immunology
*Antibodies, Monoclonal: TU, therapeutic use
Antigens, CD
Antigens, CD11: IM, immunology
Antigens, CD137
Antigens, CD8: IM, immunology
Arthritis, Rheumatoid: IM, immunology
Arthritis, Rheumatoid: PP, physiopathology
*Arthritis, Rheumatoid: TH, therapy
CD4-Positive T-Lymphocytes: IM, immunology

Collagen Type II: IM, immunology
DNA Primers
Dendritic Cells: IM, immunology
Immunohistochemistry
*Immunotherapy
Mice
Monocytes: IM, immunology
*Receptors, Nerve Growth Factor: IM, immunology
***Receptors, Tumor Necrosis Factor: IM, immunology**
Reverse Transcriptase Polymerase Chain Reaction
Spleen: IM, immunology
Tryptophan Oxygenase: IM, immunology
Tryptophan Oxygenase: ME, metabolism

CHEMICAL NAME: 0 (Antibodies, Monoclonal); 0 (Antigens, CD); 0 (Antigens, CD11); 0 (Antigens, CD137); 0 (Antigens, CD8); 0 (Collagen Type II); 0 (DNA Primers); 0 (Receptors, Nerve Growth Factor); 0 (Receptors, Tumor Necrosis Factor); 0 (TNFRSF9 protein, human); 0 (Tnfrsf9 protein, mouse); EC 1.13.11.11 (**Tryptophan Oxygenase**)

L65 ANSWER 6 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2004527608 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15498031
TITLE: Interferon-gamma-modified dendritic cells suppress B cell function and ameliorate the development of experimental autoimmune myasthenia gravis.
AUTHOR: Adikari S B; Lian H; Link H; Huang Y-M; Xiao B-G
CORPORATE SOURCE: Division of Neuroimmunology, Neurotec Department, Karolinska Institute, Stockholm, Sweden.
SOURCE: Clinical and experimental immunology, (2004 Nov) Vol. 138, No. 2, pp. 230-6.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 23 Oct 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 14 Dec 2004

ABSTRACT:
This study was designed to investigate the therapeutic effects of interferon (IFN)-gamma-modulated dendritic cells (DC) in experimental autoimmune myasthenia gravis (EAMG). We induced EAMG in Lewis rats by immunization with Torpedo nicotinic acetylcholine receptor (nAChR) and adjuvant. On day 33 post-immunization (p.i.), splenic DC were prepared, exposed to IFN-gamma alone (IFN-gamma-DC) or to IFN-gamma in combination with 1-methyl-DL-tryptophan (1-MT), the specific inhibitor of indoleamine 2,3-dioxygenase (IDO) (IFN-gamma + 1-MT-DC), and injected subcutaneously into rats with incipient EAMG on day 5 p.i. A control group of EAMG rats received naive DC on day 5 p.i., while another group received 1-MT every other day, intraperitoneally (p.i.), from days 5 to 41 p.i. The severity of clinical signs of EAMG was reduced dramatically in IFN-gamma-DC-treated rats compared to rats receiving naive DC, IFN-gamma + 1-MT-DC or 1-MT alone. The number of plasma cells secreting nAChR antibodies was reduced and the expression of B cell activation factor (BAFF) on splenic and lymph node mononuclear cells (MNC) was

down-regulated in rats treated with IFN-gamma-DC. In vitro co-culture of MNC derived from EAMG rats with IFN-gamma-DC produced relatively few cells secreting nAChR antibodies. Addition of 1-MT to the co-culture significantly increased the number of cells secreting nAChR antibodies. We conclude that IFN-gamma-DC reduced the number of plasma cells secreting nAChR antibodies in an IDO-dependent manner and ameliorated the development of EAMG in Lewis rats.

CONTROLLED TERM: Check Tags: Female
Animals
B-Cell Activating Factor
*B-Lymphocytes: IM, immunology
Cell Division: IM, immunology
*Dendritic Cells: IM, immunology
Indoleamine-Pyrrole 2,3,-Dioxygenase
*Interferon Type II: IM, immunology
Leukocytes, Mononuclear: IM, immunology
Lymph Nodes: CY, cytology
Lymph Nodes: IM, immunology
Membrane Proteins: IM, immunology
*Myasthenia Gravis, Autoimmune, Experimental: IM, immunology
Rats
Rats, Inbred Lew
Receptors, Cholinergic: IM, immunology
Spleen: CY, cytology
Spleen: IM, immunology
T-Lymphocytes: IM, immunology
*Tryptophan: AA, analogs & derivatives
Tryptophan: IM, immunology
Tryptophan Oxygenase: AI, antagonists & inhibitors
Tumor Necrosis Factor-alpha: IM, immunology

CAS REGISTRY NO.: 73-22-3 (Tryptophan); 82115-62-6 (Interferon Type II)

CHEMICAL NAME: 0 (1-**methyl-tryptophan**); 0 (B-Cell Activating Factor); 0 (Membrane Proteins); 0 (Receptors, Cholinergic); 0 (**Tumor** Necrosis Factor-alpha); EC 1.13.11.11 (**Tryptophan Oxygenase**); EC 1.13.11.42 (Indoleamine-Pyrrole 2,3,-Dioxygenase)

L65 ANSWER 7 OF 13 MEDLINE on STN

ACCESSION NUMBER: 2004077840 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 14967480

TITLE: Indoleamine 2,3-dioxygenase activity and L-tryptophan transport in human breast cancer cells.

AUTHOR: Travers M T; Gow I F; Barber M C; Thomson J; Shennan D B

CORPORATE SOURCE: Hannah Research Institute, Ayr, Scotland KA6 5HL, UK.

SOURCE: Biochimica et biophysica acta, (2004 Feb 10) Vol. 1661, No. 1, pp. 106-12.
Journal code: 0217513. ISSN: 0006-3002.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200404

ENTRY DATE: Entered STN: 18 Feb 2004
Last Updated on STN: 6 Apr 2004

Entered Medline: 5 Apr 2004

ABSTRACT:
The activity and expression of indoleamine 2,3-dioxygenase together with L-tryptophan transport has been examined in cultured human breast ***cancer*** cells. MDA-MB-231 but not MCF-7 cells expressed mRNA for indoleamine 2,3-dioxygenase. Kynurenine production by MDA-MB-231 cells, which was taken as a measure of enzyme activity, was markedly stimulated by interferon-gamma (1000 units/ml). Accordingly, L-tryptophan utilization by MDA-MB-231 cells was enhanced by interferon-gamma. 1-Methyl-DL-tryptophan (1 mM) inhibited interferon-gamma induced kynurenine production by MBA-MB-231 cells. Kynurenine production by MCF-7 cells remained at basal levels when cultured in the presence of interferon-gamma. L-Tryptophan transport into MDA-MB-231 cells was via a Na(+)-independent, BCH-sensitive pathway. It appears that system L (LAT1/CD98) may be the only pathway for l-tryptophan transport into these cells. 1-Methyl-D,L-tryptophan trans-stimulated l-tryptophan efflux from MDA-MB-231 cells and thus appears to be a transported substrate of system L. The results suggest that system L plays an important role in providing indoleamine-2,3-dioxygenase with its main substrate, L-tryptophan, and suggest a mechanism by which estrogen receptor-negative breast **cancer** cells may evade the attention of the immune system.

CONTROLLED TERM: Binding, Competitive
Breast Neoplasms: ET, etiology
Breast Neoplasms: IM, immunology
***Breast Neoplasms: ME, metabolism**
Cell Line, Tumor
Culture Media, Conditioned: AN, analysis
Humans
Interferon Type II: PD, pharmacology
Norbornanes: PD, pharmacology
RNA, Messenger: BI, biosynthesis
Receptors, Estrogen: ME, metabolism
*Tryptophan: AA, analogs & derivatives
Tryptophan: AN, analysis
*Tryptophan: ME, metabolism
Tryptophan: PD, pharmacology
Tryptophan Oxygenase: AI, antagonists & inhibitors
Tryptophan Oxygenase: BI, biosynthesis
***Tryptophan Oxygenase: ME, metabolism**

CAS REGISTRY NO.: 73-22-3 (Tryptophan); 82115-62-6 (Interferon Type II)

CHEMICAL NAME: 0 (1-**methyl-tryptophan**); 0 (Culture Media, Conditioned); 0 (Norbornanes); 0 (RNA, Messenger); 0 (Receptors, Estrogen); EC 1.13.11.11 (**Tryptophan Oxygenase**)

L65 ANSWER 8 OF 13 MEDLINE on STN

ACCESSION NUMBER: 2003458718 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 14520367

TITLE: **Tumors** hijack fetal enzyme, escape killer T cells.

AUTHOR: Schepers Koen; Schumacher Ton N M

SOURCE: Nature medicine, (2003 Oct) Vol. 9, No. 10, pp. 1253-4.
Journal code: 9502015. ISSN: 1078-8956.

COMMENT: Comment on: Nat Med. 2003 Oct;9(10):1269-74. PubMed ID: 14502282

PUB. COUNTRY: United States

DOCUMENT TYPE: Commentary

News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 22 Jan 2004
Entered Medline: 21 Jan 2004
CONTROLLED TERM: Check Tags: Female
Animals
Fetus: IM, immunology
Fetus: PH, physiology
Humans
Mice
Neoplasms: IM, immunology
***Neoplasms: ME, metabolism**
Placenta: ME, metabolism
Pregnancy
T-Lymphocytes, Cytotoxic: IM, immunology
*T-Lymphocytes, Cytotoxic: ME, metabolism
Tryptophan: AD, administration & dosage
*Tryptophan: AA, analogs & derivatives
*Tryptophan: ME, metabolism
Tryptophan: PD, pharmacology
***Tryptophan Oxygenase: ME, metabolism**
Tumor Escape
CAS REGISTRY NO.: **13510-08-2 (alpha-methyltryptophan)**;
73-22-3 (Tryptophan)
CHEMICAL NAME: EC 1.13.11.11 (**Tryptophan Oxygenase**
)

L65 ANSWER 9 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2003458697 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14502282
TITLE: Evidence for a tumoral immune resistance mechanism based on tryptophan degradation by indoleamine 2,3-dioxygenase.
AUTHOR: Uyttenhove Catherine; Pilotte Luc; Theate Ivan; Stroobant Vincent; Colau Didier; Parmentier Nicolas; Boon Thierry; Van den Eynde Benoit J
CORPORATE SOURCE: Ludwig Institute for Cancer Research and Cellular Genetics Unit, Universite de Louvain, B-1200 Brussels, Belgium.
SOURCE: Nature medicine, (2003 Oct) Vol. 9, No. 10, pp. 1269-74. Electronic Publication: 2003-09-21.
Journal code: 9502015. ISSN: 1078-8956.
COMMENT: Comment in: Nat Med. 2003 Oct;9(10):1253-4. PubMed ID: 14520367
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 22 Jan 2004
Entered Medline: 21 Jan 2004

ABSTRACT:
T lymphocytes undergo proliferation arrest when exposed to tryptophan shortage, which can be provoked by indoleamine 2,3-dioxygenase (IDO), an enzyme that is expressed in placenta and catalyzes tryptophan

degradation. Here we show that most human tumors constitutively express IDO. We also observed that expression of IDO by immunogenic mouse tumor cells prevents their rejection by preimmunized mice. This effect is accompanied by a lack of accumulation of specific T cells at the tumor site and can be partly reverted by systemic treatment of mice with an inhibitor of IDO, in the absence of noticeable toxicity. These results suggest that the efficacy of therapeutic vaccination of cancer patients might be improved by concomitant administration of an IDO inhibitor.

CONTROLLED TERM: Check Tags: Female
Animals
*CD8-Positive T-Lymphocytes: IM, immunology
Cell Line, Tumor
Humans
Indoleamine-Pyrrole 2,3,-Dioxygenase
Mice
Neoplasm Transplantation
Neoplasms: IM, immunology
*Neoplasms: ME, metabolism
Neoplasms: PA, pathology
Placenta: EN, enzymology
Pregnancy
RNA, Messenger: ME, metabolism
*Tryptophan: AA, analogs & derivatives
*Tryptophan: ME, metabolism
Tryptophan: PD, pharmacology
Tryptophan Oxygenase: AI, antagonists & inhibitors
Tryptophan Oxygenase: GE, genetics
*Tryptophan Oxygenase: ME, metabolism
*Tumor Escape

CAS REGISTRY NO.: 13510-08-2 (alpha-methyltryptophan); 73-22-3 (Tryptophan)

CHEMICAL NAME: 0 (RNA, Messenger); EC 1.13.11.11 (Tryptophan Oxygenase); EC 1.13.11.42 (Indoleamine-Pyrrole 2,3,-Dioxygenase)

L65 ANSWER 10 OF 13 MEDLINE on STN

ACCESSION NUMBER: 2003597390 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 14678522

TITLE: Inhibition of indoleamine 2,3-dioxygenase suppresses NK cell activity and accelerates tumor growth.

AUTHOR: Kai Seiichiro; Goto Shigeru; Tahara Kouichirou; Sasaki Atsushi; Kawano Katsunori; Kitano Seigo

CORPORATE SOURCE: Department of Surgery I, Oita University Faculty of Medicine, Oita, Japan.

SOURCE: Journal of experimental therapeutics & oncology, (2003 Nov-Dec) Vol. 3, No. 6, pp. 336-45. Journal code: 9604933. ISSN: 1359-4117.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200403

ENTRY DATE: Entered STN: 18 Dec 2003
Last Updated on STN: 30 Mar 2004
Entered Medline: 29 Mar 2004

ABSTRACT:

Indoleamine 2,3-dioxygenase (IDO), a tryptophan catabolizing enzyme, is induced under various pathological conditions, including viral and bacterial infection, allograft rejection, cerebral ischemia, and ***tumor*** growth. We have previously reported that the expression of IDO mRNA was increased in some clinical cases of hepatocellular carcinoma in which the recurrence-free survival rate in these IDO-positive patients was significantly higher than that in patients without IDO mRNA induction in tumors. Additionally, IDO expressed in tumors was localized not to the tumor cells but instead to tumor -infiltrating cells by immunohistochemistry. In this study, in order to elucidate the mechanisms underlying anti-tumor effect of IDO, we investigated whether IDO inhibitor (1-methyl-dl-tryptophan, 1MT) affects the growth of subcutaneous B16 tumors in mice. Subsequently, the activity of natural killer (NK) cells was investigated under the conditions of inhibited IDO activity in vivo and in vitro. IDO mRNA expression of B16 cells, B16 subcutaneous tumor, sprenocytes of mice, and human NK cells were studied by reverse transcription-polymerase chain reaction. B16 subcutaneous tumor growth with or without IDO inhibition was observed and cytotoxic activity of NK cells were investigated under the conditions of inhibited IDO activity in vivo and in vitro. IDO mRNA was expressed in B16 subcutaneous tumor, splenocytes of tumor bearing mice, co-cultured splenocytes with B16, and human NK cells. On day 14, after injection of B16 melanoma cells, the sizes of ***tumors*** in IDO-inhibited mice were significantly larger than those in control mice. The cytotoxic activity of mice NK cells was reduced by IDO inhibition in vivo. In vitro inhibition of IDO, NK activity was reduced in dose-dependent manner of 1MT. In conclusion, these results indicated that IDO plays an important role in anti-tumor immunity by regulating cytotoxic activity of NK cells.

CONTROLLED TERM: Check Tags: Male
Animals
Cell Line, Tumor: DE, drug effects
Dose-Response Relationship, Drug
Humans
Immunohistochemistry
Indoleamine-Pyrrole 2,3,-Dioxygenase
*Killer Cells, Natural: DE, drug effects
Killer Cells, Natural: EN, enzymology
Killer Cells, Natural: IM, immunology
Melanoma: EN, enzymology
Melanoma: IM, immunology
Mice
Mice, Inbred C57BL
RNA, Messenger: AN, analysis
Reverse Transcriptase Polymerase Chain Reaction
Tryptophan: AD, administration & dosage
*Tryptophan: AA, analogs & derivatives
*Tryptophan: PD, pharmacology
***Tryptophan Oxygenase: DE, drug effects**
Tryptophan Oxygenase: ME, metabolism

CAS REGISTRY NO.: 73-22-3 (Tryptophan); 7303-49-3 (methyl tryptophan)

CHEMICAL NAME: 0 (RNA, Messenger); EC 1.13.11.11 (Tryptophan Oxygenase); EC 1.13.11.42 (Indoleamine-Pyrrole 2,3,-Dioxygenase)

L65 ANSWER 11 OF 13 MEDLINE on STN
ACCESSION NUMBER: 81142116 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7204339

TITLE: Involvement of plasmid deoxyribonucleic acid in indoleacetic acid synthesis in Pseudomonas savastanoi.
AUTHOR: Comai L; Kosuge T
SOURCE: Journal of bacteriology, (1980 Aug) Vol. 143, No. 2, pp. 950-7.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198105
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 16 Mar 1990
Entered Medline: 21 May 1981

ABSTRACT:
Olive (or oleander) knot is a plant disease incited by Pseudomonas savastanoi. Disease symptoms consist of tumorous outgrowths induced in the plant by bacterial production of indole-3-acetic acid (IAA). Synthesis of IAA occurs by the following reactions: L-tryptophan leads to indoleacetamide leads to indoleacetic acid, catalyzed by tryptophan 2-monooxygenase and indoleacetamide hydrolase, respectively. Whereas the enzymology of IAA synthesis is well characterized, nothing is known about the genetics of the system. We devised a positive selection for the presence of tryptophan 2-monooxygenase based on its capacity to use as a substrate the toxic tryptophan analogue 5-***methyltryptophan.*** Efficient curing of the bacterium of tryptophan 2-monoxygenase, indoleacetamide hydrolase, and IAA production was obtained by acridine orange treatment. Further, loss of capacity to produce IAA by curing was correlated with loss of a plasmid of 34 X 10(6) molecular weight. This plasmid, here called pIAA1, when reintroduced into Iaa- mutants by transformation, restored tryptophan 2-monooxygenase and indoleacetamide hydrolase activities and production of IAA.

CONTROLLED TERM: Acridine Orange: PD, pharmacology
Amidohydrolases: GE, genetics
DNA, Bacterial: GE, genetics
*Indoleacetic Acids: BI, biosynthesis
*Plasmids
*Pseudomonas: GE, genetics
Transformation, Genetic
Tryptophan Hydroxylase: AI, antagonists & inhibitors
Tryptophan Hydroxylase: GE, genetics
CAS REGISTRY NO.: 65-61-2 (Acridine Orange)
CHEMICAL NAME: 0 (DNA, Bacterial); 0 (Indoleacetic Acids); EC 1.14.16.4 (**Tryptophan Hydroxylase**); EC 3.5.- (Amidohydrolases); EC 3.5.1.- (indoleacetamide hydrolase)

L65 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:495867 BIOSIS Full-text
DOCUMENT NUMBER: PREV200510265986
TITLE: Linking two immuno-suppressive molecules: Indoleamine 2,3 dioxygenase can modify HLA-G cell-surface expression.
AUTHOR(S): Gonzalez-Hernandez, Alvaro; LeMaoult, Joel [Reprint Author]; Lopez, Ana; Alegre, Estibaliz; Caumartin, Julien; Le Rond, Solne; Daouya, Marina; Moreau,

Philippe; Carosella, Edgardo D.
CORPORATE SOURCE: Univ Navarra Clin, Navarra 31080, Spain
lemaoult@dsvidf.cea.fr
SOURCE: Biology of Reproduction, (SEP 2005) Vol. 73, No. 3, pp. 571-578.
CODEN: BIREBV. ISSN: 0006-3363.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005
ABSTRACT:Nonclassical human leukocyte antigen (HLA) class I molecule HLA-G and indoleamine 2,3 dioxygenase (**INDO**) in humans and mice, respectively, have been shown to play crucial immunosuppressive roles in fetal-maternal tolerance. HLA-G inhibits natural killer and T cell function by high-affinity interaction with inhibitory receptors, and ***INDO*** acts by depleting the surrounding microenvironment of the essential amino acid tryptophan, thus inhibiting T cell proliferation. We investigated whether HLA-G expression and **INDO** function were linked. Working with antigen-presenting cell (APC) lines and monocytes, we found that functional inhibition of **INDO** by 1-**methyl -tryptophan** induced cell surface expression of HLA-G1 by HLA-G1-negative APCs that were originally cell-surface negative, and that in reverse, the functional boost of **INDO** by high concentrations of tryptophan induced a complete loss of HLA-G1 cell surface expression by APCs that were originally cell-surface HLA-G1-positive. This mechanism was shown to be post-translational because HLA-G protein cell contents remained unaffected by the treatments used. Furthermore, HLA-G cell surface expression regulation by **INDO** seems to relate to ***INDO*** function, but not to tryptophan catabolism itself. Potential implications in fetal-maternal tolerance are discussed.
CONCEPT CODE: Cytology - General 02502
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Immunological processes and allergy 22018
Immunology - General and methods 34502
INDEX TERMS: Major Concepts
Pharmacology; Immune System (Chemical Coordination and Homeostasis); Cell Biology
INDEX TERMS: Parts, Structures, & Systems of Organisms
monocyte: immune system, blood and lymphatics; T-cell: immune system, blood and lymphatics; natural killer cell: immune system, blood and lymphatics; antigen-presenting cell: immune system
INDEX TERMS: Chemicals & Biochemicals
tryptophan; inhibitory receptors; 1-**methyl -tryptophan**; human leukocyte antigen class I molecule [HLA-G]: immunologic-drug, immunosuppressant-drug; indoleamine 2,3 dioxygenase: immunologic-drug, immunosuppressant-drug
INDEX TERMS: Miscellaneous Descriptors
fetal maternal tolerance

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
U937 cell line (cell_line): human histiocytic lymphoma cells
FON cell line (cell_line)
JEG-3 cell line (cell_line)
THP-1 cell line (cell_line): human acute monocytic leukemia cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
M8 cell line (cell_line)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
REGISTRY NUMBER: 73-22-3 (tryptophan)
21339-55-9 (1-methyl-tryptophan)

L65 ANSWER 13 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006041842 EMBASE Full-text
TITLE: Monitoring tryptophan metabolism in chronic immune activation.
AUTHOR: Schrocksnadel K.; Wirleitner B.; Winkler C.; Fuchs D.
CORPORATE SOURCE: Dietmar.Fuchs@uibk.ac.at
SOURCE: Clinica Chimica Acta, (2006) Vol. 364, No. 1-2, pp. 82-90. .
Refs: 76
ISSN: 0009-8981 CODEN: CCATAR
PUBLISHER IDENT.: S 0009-8981(05)00478-X
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006

ABSTRACT: The essential amino acid tryptophan is a constituent of proteins and is also a substrate for two important biosynthetic pathways: the generation of neurotransmitter 5-hydroxytryptamine (serotonin) by tryptophan 5-hydroxylase, and the formation of kynurenine derivatives and nicotinamide adenine dinucleotides. The latter pathway is initiated by the enzymes tryptophan pyrrolase (tryptophan ***2*** ,3-dioxygenase, TDO) and indoleamine 2,3-dioxygenase (IDO). TDO is located in liver cells, whereas IDO is expressed in a variety of cells including monocyte-derived macrophages and dendritic cells and is preferentially induced by Th1-type cytokine interferon-γ. Tryptophan depletion via IDO is part of the cytostatic and antiproliferative activity mediated by interferon-γ

in cells. In vivo tryptophan concentration can be measured by HPLC by monitoring its natural fluorescence (285 nm excitation and 365 nm emission wavelength). IDO activity is characterized best by the kynurenine to tryptophan ratio which correlates with concentrations of immune activation markers such as neopterin. Low serum/plasma tryptophan concentration is observed in infectious, autoimmune, and malignant diseases and disorders that involve cellular (Th1-type) immune activation as well as during pregnancy due to accelerated tryptophan conversion. Thus, in states of persistent immune activation, low tryptophan concentration may contribute to immunodeficiency. Decreased serum tryptophan can also effect serotonin biosynthesis and thus contribute to impaired quality of life and depressive mood. As such, monitoring tryptophan metabolism in chronic immunopathology provides a better understanding of the association between immune activation and IDO and its role in the development of immunodeficiency, anemia and mood disorders.

CONTROLLED TERM: Medical Descriptors:
*tryptophan metabolism
*immune response
immune deficiency
protein localization
liver cell
macrophage
dendritic cell
high performance liquid chromatography
amino acid blood level
infection
autoimmune disease
cancer
pregnancy
depression
anemia
mood disorder: DT, drug therapy
immunostimulation
cachexia
amino acid deficiency: DT, drug therapy
tryptophan deficiency: DT, drug therapy
drug inhibition
highly active antiretroviral therapy
human
nonhuman
review
priority journal
Drug Descriptors:
tryptophan: EC, endogenous compound
serotonin: EC, endogenous compound
tryptophan hydroxylase: EC, endogenous compound
kynurenine: EC, endogenous compound
nicotinamide adenine dinucleotide: EC, endogenous compound
tryptophan 2,3 dioxygenase: EC, endogenous compound
indoleamine 2,3 dioxygenase: EC, endogenous compound
gamma interferon
nicotinamide: DT, drug therapy
serotonin uptake inhibitor: DT, drug therapy
serotonin uptake inhibitor: PD, pharmacology
tryptophan derivative: PD, pharmacology

1 methyl tryptophan: PD, pharmacology
tryptophan beta (3 benzofuranyl)alanine: PD, pharmacology
alanine derivative: PD, pharmacology
beta [3 benzo(b)thienyl]alanine: PD, pharmacology
acetylsalicylic acid: PD, pharmacology
Hypericum perforatum extract: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (tryptophan) 6912-86-3, 73-22-3; (serotonin) 50-67-9; (tryptophan hydroxylase) 9037-21-2; (kynurenine) 16055-80-4, 343-65-7; (nicotinamide adenine dinucleotide) 53-84-9; (tryptophan 2,3 dioxygenase) 9014-51-1; (gamma interferon) 82115-62-6; (nicotinamide) 11032-50-1, 98-92-0; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1

CHEMICAL NAME: Aspirin

SEARCH RESULTS

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=> d his nofile

     (FILE 'HOME' ENTERED AT 10:57:10 ON 12 SEP 2007)

     FILE 'HCAPLUS' ENTERED AT 13:00:49 ON 12 SEP 2007
                E US20050186289/PN
L9              1 SEA ABB=ON  PLU=ON  US2005186289/PN
                  SEL RN

     FILE 'REGISTRY' ENTERED AT 13:01:07 ON 12 SEP 2007
L10            28 SEA ABB=ON  PLU=ON  (110117-83-4/BI OR 111139-55-0/BI OR
                  147-94-4/BI OR 15663-27-1/BI OR 1956-23-6/BI OR 21339-55-
                  9/BI OR 23214-92-8/BI OR 26988-72-7/BI OR 36802-39-8/BI
                  OR 3778-73-2/BI OR 50-18-0/BI OR 51-21-8/BI OR 55-98-1/BI
                   OR 56937-50-9/BI OR 57-22-7/BI OR 59-05-2/BI OR
                  72071-49-9/BI OR 793717-08-5/BI OR 796082-20-7/BI OR
                  796636-60-7/BI OR 796636-61-8/BI OR 796636-62-9/BI OR
                  796636-63-0/BI OR 796636-64-1/BI OR 796636-65-2/BI OR
                  83869-56-1/BI OR 9014-51-1/BI OR 95058-81-4/BI)

     FILE 'HCAPLUS' ENTERED AT 13:01:19 ON 12 SEP 2007
L11             1 SEA ABB=ON  PLU=ON  L9 AND L10

     FILE 'REGISTRY' ENTERED AT 13:05:15 ON 12 SEP 2007
L12             1 SEA ABB=ON  PLU=ON  21339-55-9/RN
L13             1 SEA ABB=ON  PLU=ON  26988-72-7/RN
L14             1 SEA ABB=ON  PLU=ON  110117-83-4/RN
L15             3 SEA ABB=ON  PLU=ON  L12 OR L13 OR L14
L16             1 SEA ABB=ON  PLU=ON  9014-51-1/RN

     FILE 'HCAPLUS' ENTERED AT 13:59:40 ON 12 SEP 2007
L17           637 SEA ABB=ON  PLU=ON  L15 OR METHYLTRYPTOPHAN/OBI OR
                  METHYL/OBI(W)TRYPTOPHAN/OBI
L18          8041 SEA ABB=ON  PLU=ON  L16 OR TDO/OBI(W)DIOXYGENASE/OBI OR
                  TRYPTOPHAN/OBI(W)(PYRROLASE/OBI OR HYDROXYLASE/OBI OR
                  DIOXYGENASE/OBI OR PEROXIDASE/OBI OR OXYGENASE/OBI)OR
                  INDOLEMINE/OBI(W)DIOXYGENASE/OBI OR TRYPTOPHAN/OBI(W)2/OB
                  I(W)3/OBI(W)DIOXYGENASE/OBI OR INDO/OBI
L19        677089 SEA ABB=ON  PLU=ON  CANCER?/OBI OR MELANOMA?/OBI OR
                  SARCOMA?/OBI OR NEOPLASM?/OBI OR LYMPHOMA?/OBI OR
                  TUMOR?/OBI
L20            39 SEA ABB=ON  PLU=ON  L17 AND L18
L21            12 SEA ABB=ON  PLU=ON  L20 AND L19
L24           290 SEA ABB=ON  PLU=ON  MELLOR A?/AU
L25            44 SEA ABB=ON  PLU=ON  L23 AND L24
L26            32 SEA ABB=ON  PLU=ON  L25 AND L18
L27             5 SEA ABB=ON  PLU=ON  L26 AND L17
L28             4 SEA ABB=ON  PLU=ON  L22 NOT L27

     FILE 'WPIX' ENTERED AT 14:17:28 ON 12 SEP 2007
L29            85 SEA ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR METHYL(W)TRYPTOPH
                  AN
L30           363 SEA ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR TRYPTOPHAN(W)(PY
                  RROLASE OR HYDROXYLASE OR DIOXYGENASE OR PEROXIDASE OR
                  OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR TRYPTOPHAN(W)2(W
                  )3(W)DIOXYGENASE OR INDO
L31        109203 SEA ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR SARCOMA? OR
                  NEOPLASM? OR LYMPHOMA? OR TUMOR?
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L32           0 SEA ABB=ON  PLU=ON  L29 AND L30
L33          14 SEA ABB=ON  PLU=ON  L23 AND L24
L34           6 SEA ABB=ON  PLU=ON  L33 AND L29
L35           4 SEA ABB=ON  PLU=ON  L34 AND (1840-2003)/PRY,PY,AY

     FILE 'JAPIO' ENTERED AT 14:22:33 ON 12 SEP 2007
L36           5 SEA ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR METHYL(W)TRYPTOPH
                AN
L37          18 SEA ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR TRYPTOPHAN(W)(PY
                RROLASE OR HYDROXYLASE OR DIOXYGENASE OR PEROXIDASE OR
                OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR TRYPTOPHAN(W)2(W
                )3(W)DIOXYGENASE OR INDO
L38           0 SEA ABB=ON  PLU=ON  L36 AND L37
L39           0 SEA ABB=ON  PLU=ON  L23 AND L24

     FILE 'MEDLINE' ENTERED AT 14:23:19 ON 12 SEP 2007
L40         461 SEA ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR METHYL(W)TRYPTOPH
                AN
L41        6818 SEA ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR TRYPTOPHAN(W)(PY
                RROLASE OR HYDROXYLASE OR DIOXYGENASE OR PEROXIDASE OR
                OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR TRYPTOPHAN(W)2(W
                )3(W)DIOXYGENASE OR INDO
L42          51 SEA ABB=ON  PLU=ON  L40 AND L41
L43     1982664 SEA ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR SARCOMA? OR
                NEOPLASM? OR LYMPHOMA? OR TUMOR?
L44           8 SEA ABB=ON  PLU=ON  L42 AND L43
L45          37 SEA ABB=ON  PLU=ON  L23 AND L24
L46           5 SEA ABB=ON  PLU=ON  L45 AND L29
L47           7 SEA ABB=ON  PLU=ON  L44 NOT L46

     FILE 'BIOSIS' ENTERED AT 14:24:36 ON 12 SEP 2007
L48         616 SEA ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR METHYL(W)TRYPTOPH
                AN
L49       13004 SEA ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR TRYPTOPHAN(W)(PY
                RROLASE OR HYDROXYLASE OR DIOXYGENASE OR PEROXIDASE OR
                OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR TRYPTOPHAN(W)2(W
                )3(W)DIOXYGENASE OR INDO
L50          17 SEA ABB=ON  PLU=ON  L48 AND L49
L51     1583882 SEA ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR SARCOMA? OR
                NEOPLASM? OR LYMPHOMA? OR TUMOR?
L52           2 SEA ABB=ON  PLU=ON  L50 AND L51
L53          46 SEA ABB=ON  PLU=ON  L23 AND L24
L54           3 SEA ABB=ON  PLU=ON  L53 AND L29
L55           1 SEA ABB=ON  PLU=ON  L52 NOT L54

     FILE 'EMBASE' ENTERED AT 14:25:35 ON 12 SEP 2007
L56         547 SEA ABB=ON  PLU=ON  METHYLTRYPTOPHAN OR METHYL(W)TRYPTOPH
                AN
L57        5445 SEA ABB=ON  PLU=ON  TDO(W)DIOXYGENASE OR TRYPTOPHAN(W)(PY
                RROLASE OR HYDROXYLASE OR DIOXYGENASE OR PEROXIDASE OR
                OXYGENASE)OR INDOLEMINE(W)DIOXYGENASE OR TRYPTOPHAN(W)2(W
                )3(W)DIOXYGENASE OR INDO
L58          24 SEA ABB=ON  PLU=ON  L56 AND L57
L59     1446540 SEA ABB=ON  PLU=ON  CANCER? OR MELANOMA? OR SARCOMA? OR
                NEOPLASM? OR LYMPHOMA? OR TUMOR?
L60           2 SEA ABB=ON  PLU=ON  L58 AND L59
L61          37 SEA ABB=ON  PLU=ON  L23 AND L24
L62           5 SEA ABB=ON  PLU=ON  L61 AND L29
L63           1 SEA ABB=ON  PLU=ON  L60 NOT L62
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     FILE 'HCAPLUS' ENTERED AT 14:46:53 ON 12 SEP 2007
               D QUE NOS L27

     FILE 'WPIX' ENTERED AT 14:47:03 ON 12 SEP 2007
               D QUE NOS L34

     FILE 'JAPIO' ENTERED AT 14:47:14 ON 12 SEP 2007
               D QUE NOS L39

     FILE 'MEDLINE' ENTERED AT 14:47:24 ON 12 SEP 2007
               D QUE NOS L46

     FILE 'BIOSIS' ENTERED AT 14:47:44 ON 12 SEP 2007
               D QUE NOS L54

     FILE 'EMBASE' ENTERED AT 14:47:54 ON 12 SEP 2007
               D QUE NOS L62

     FILE 'HCAPLUS, MEDLINE, BIOSIS, WPIX, EMBASE' ENTERED AT 14:48:29
     ON 12 SEP 2007
L64           15 DUP REM L27 L46 L54 L34 L62 (9 DUPLICATES REMOVED)
                    ANSWERS '1-5' FROM FILE HCAPLUS
                    ANSWERS '6-10' FROM FILE MEDLINE
                    ANSWER '11' FROM FILE BIOSIS
                    ANSWERS '12-13' FROM FILE WPIX
                    ANSWERS '14-15' FROM FILE EMBASE
               D QUE L64
               D IBIB ABS L64 1-15

     FILE 'HCAPLUS' ENTERED AT 14:51:04 ON 12 SEP 2007
               D QUE NOS L28

     FILE 'WPIX' ENTERED AT 14:51:15 ON 12 SEP 2007
               D QUE NOS L32

     FILE 'JAPIO' ENTERED AT 14:51:25 ON 12 SEP 2007
               D QUE NOS L38

     FILE 'MEDLINE' ENTERED AT 14:51:35 ON 12 SEP 2007
               D QUE NOS L47

     FILE 'BIOSIS' ENTERED AT 14:51:45 ON 12 SEP 2007
               D QUE NOS L55

     FILE 'EMBASE' ENTERED AT 14:51:57 ON 12 SEP 2007
               D QUE NOS L63

     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:52:32 ON 12
     SEP 2007
L65           13 DUP REM L28 L47 L55 L63 (0 DUPLICATES REMOVED)
                    ANSWERS '1-4' FROM FILE HCAPLUS
                    ANSWERS '5-11' FROM FILE MEDLINE
                    ANSWER '12' FROM FILE BIOSIS
                    ANSWER '13' FROM FILE EMBASE
               D QUE NOS L65
               D L65 IBIB ABS HITRN 1-4
               D L65 5-13 IALL

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